DOI:
10.14309/ajg.0000000000000267

Document Version
Peer reviewed version

Perceptions of constipation among the general public and people with constipation differ strikingly from those of general and specialist doctors and the Rome IV criteria

Eirini Dimidi, Camilla Cox, Robert Grant, S. Mark Scott, Kevin Whelan

AFFILIATIONS:

Eirini Dimidi, BSc MSc PhD, King's College London, Department of Nutritional Sciences, London, United Kingdom; eirini.dimidi@kcl.ac.uk

Camilla Cox, BSc MSc, King's College London, Department of Nutritional Sciences, London, United Kingdom; camillacox25@gmail.com

Robert Grant, BSc MSc, BayesCamp Ltd; Honorary Research Fellow, Kingston University and St George's, University of London, Faculty of Health, Social Care & Education, Kingston upon Thames, United Kingdom; robert@bayescamp.com

S. Mark Scott, BSc PhD, Wingate Institute for Neurogastroenterology, Centre for Neuroscience and Trauma, Blizard Institute, Queen Mary University of London, London, United Kingdom; m.scott@qmul.ac.uk

Kevin Whelan, BSc MSc MA PhD, King's College London, Department of Nutritional Sciences, London, United Kingdom; kevin.whelan@kcl.ac.uk

CORRESPONDING AUTHOR: Professor Kevin Whelan, King's College London, Franklin Wilkins Building, 150 Stamford Street, London, United Kingdom, SE1 9NH, kevin.whelan@kcl.ac.uk, tel: +44 (0)20 7848 3858.

GUARANTOR OF THE ARTICLE: Professor Kevin Whelan, King's College London, Franklin Wilkins Building, 150 Stamford Street, London, United Kingdom, SE1 9NH, kevin.whelan@kcl.ac.uk, tel: +44 (0)20 7848 3858.

SPECIFIC AUTHOR CONTRIBUTIONS: The study was designed by ED, SMS and KW. The sample size calculation was performed by ED. Participant recruitment and data entry was undertaken by ED and CC. ED, SMS and KW distributed the questionnaire to Specialist doctors. The statistical analysis was undertaken by ED and RG, and data interpretation was performed ED, RG, SMS and KW. ED wrote the initial manuscript. CC, RG, SMS and KW critically revised the manuscript. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

ACKNOWLEDGMENTS: We would like to thank Dr Yanzhong Wang (Statistician, King's College London) for assistance with sample size calculation. We would also like to thank Prof Charles Knowles and Prof James Lindsay for assistance distributing questionnaires to specialist doctors, and Susan Neville who contributed to recruitment and data collection.

FINANCIAL SUPPORT: This survey was completed as part of a PhD studentship funded by Nestec Ltd. However, Nestec Ltd had no involvement in the design, implementation, data analysis and interpretation of the survey, nor the preparation of this manuscript.

POTENTIAL COMPETING INTERESTS: None

SHORT TITLE: Perceptions of constipation diagnosis

WORD COUNT: 5,198

ABSTRACT

Objective: To compare the perceptions of constipation among the general population (with and without constipation), general and specialist doctors and the Rome IV criteria.

Methods: A cross-sectional survey using a self-administered questionnaire where participants were asked to report symptoms perceived to be most important for a diagnosis of constipation. Participants also judged 10 case studies in which constipation was either present or absent according to Rome IV criteria.

Results: 2,557 members of the general population (934 with self-reported constipation, 1,623 without constipation), 411 general practitioners (GPs) and 365 gastroenterology specialists completed the questionnaire. Of the 934 with self-reported constipation, 877 (94%) met Rome IV criteria for functional constipation, whereas of the 1,623 who did not self-report constipation, 473 (29%) actually met Rome IV criteria. Infrequent bowel movements were perceived as important for diagnosing constipation by less than a third of the constipated general population (26%), compared with 41% of GPs and 65% of specialist doctors ($p<0.001$). Principal component analysis revealed seven symptom clusters, with most symptoms not being part of formal diagnostic criteria. Using case studies, correct diagnosis of constipation ranged from 99% down to as low as 39%, depending upon the number and type of symptom present.

Conclusion: The general population's perceptions of constipation differ strikingly from those of GPs and specialist doctors, and there is limited agreement between public perceptions of constipation and Rome IV criteria. These findings emphasize the need to educate doctors and the general population regarding the symptoms of constipation, and re-align diagnostic criteria to address those symptoms patients perceive to be important.

STUDY HIGHLIGHTS

1. **What is current knowledge?**
   - Constipation is a common, bothersome disorder representing a huge social and healthcare burden.
   - Findings from previous studies suggest a disagreement in perceptions of constipation diagnosis among the general population and doctors and the Rome criteria.
2. **What is new here?**
   - There are differences in the symptoms considered important to a diagnosis of constipation between the general population, GPs and gastroenterology specialists, and there is variable agreement with the Rome IV criteria.
   - Infrequent bowel movements were most frequently reported as important by specialist doctors compared with less than half of GPs and less than a third of the constipated general population.
   - Seven clusters of symptoms important for a diagnosis were identified, with the majority of the symptoms included not being part of formal diagnostic criteria.
   - In 10 case studies describing the presence/absence of constipation, the absence of constipation was correctly identified by doctors in 85-92% of the cases without constipation, whereas the presence of constipation was correctly identified in only 60-70% of the cases with constipation.

INTRODUCTION

Constipation is a common problematic condition, representing a large socioeconomic burden; it impacts significantly on healthcare resources, despite the fact that the majority of patients with chronic constipation do not visit a doctor regarding their symptoms [1]. In the United States (US) alone, 3 million patients per year visit medical care centres with a primary complaint of constipation [2], with an annual direct cost of up to $7,522 per patient [3], whilst in the United Kingdom (UK), there are more than 1 million general practitioner (GP; primary care physician) consultations and 63,427 hospital admissions per year where constipation is a diagnosis [4, 5].

Nevertheless, terminology, definitions, criteria, and approaches to diagnosis of constipation are fraught with variability.

Firstly, the terminology used to characterise constipation in the medical literature varies considerably. 'Chronic constipation' usually refers to the presence of constipation-related symptoms over a long period of time [6], 'functional constipation' refers to 'chronic constipation' in the absence of any physiological or anatomical abnormalities[7], 'refractory constipation' refers to 'functional constipation' where response to management is suboptimal[8], whilst 'constipation-predominant irritable bowel syndrome' refers to 'functional constipation' with coexistent abdominal pain associated with defecation or a change in bowel habits[7]. These terminologies may provide some distinction for research purposes but are rarely used to phenotype patients in clinical practice[9].

Secondly, the approach to diagnosing constipation can vary. People can self-diagnose based upon specific symptoms they experience and which they perceive to be associated with constipation. Some may self-manage and some may then present to a doctor such as a General Practitioner (GP)/Family Physician or specialist doctor in gastroenterology or colorectal surgery. Such doctors may investigate and diagnose constipation pragmatically, based on the assessment of a broad range of symptoms, such as difficult and/or infrequent defecations, or they may use formal diagnostic criteria, such as the Rome criteria, the Cleveland Clinic Constipation Score, or the Patient Assessment of Constipation

Symptoms (PAC-SYM)[7, 10, 11]. For example, the most recent iteration of the Rome criteria, the Rome IV criteria, specify that a patient must have at least two of the following symptoms for three months or longer with onset of symptoms at least six months prior to diagnosis: (a) straining during >25% of defecations; (b) lumpy or hard stools in >25% of defecations; (c) sensation of incomplete evacuation for >25% of defecations; (d) sensation of anorectal obstruction/blockage for >25% of defecations; (e) manual maneuvres to facilitate >25% of defecations; (f) fewer than three defecations per week [7].

A meta-analysis of epidemiological studies has reported a pooled prevalence of chronic constipation in the general population of 14%, but with remarkable variation ranging from 2.9% to 35%[12]. The heterogeneity in prevalence is the result of the variations in diagnostic approach described, with self-reporting constipation resulting in the highest pooled prevalence (15%), compared to using the formal diagnostic criteria which results in declining pooled prevalence: Rome I (14%); Rome II (11%); and Rome III (7%)[12]; with a recent study showing Rome IV resulted in an even lower prevalence (6.3%)[13].

The symptoms perceived to constitute constipation are therefore important as they impact the diagnosis and management behaviour of both the general public (e.g. self-diagnosis and self-management; presentation to a doctor) and doctors (e.g. use of pragmatic diagnosis; formal diagnostic criteria) and also because they impact prevalence reports where these methods are used to define constipation.

However, there are variations in the perceptions of constipation among the general population and GPs[14]. A US study that included 100 primary care physicians showed that they appear to focus on stool frequency and consistency only and do not typically use the Rome criteria in clinical practice[15]. Likewise, the general public frequently use symptoms not included in the Rome criteria or the Cleveland Clinic Constipation Score to characterize constipation, including laxative use and pain during defecation [16-18]. Such discrepancies in perceptions of constipation may not only impact prevalence rates, but may also directly influence patient access to care and management. Correct diagnosis is fundamental to appropriate therapeutic approach. Accordingly, despite several treatment options

available for constipation, patient satisfaction is limited; for example initial constipation treatment using either over-the-counter or prescription medication reportedly fails in 49% and 58% of patients, respectively[19], and almost half of patients are not completely satisfied with their current constipation treatment [20].

In view of these findings, the aim was to assess and compare the perceptions of the symptoms of constipation among the general population (with and without constipation), and both general and specialist doctors and the Rome IV criteria.

METHODS

This was a prospective, cross-sectional survey using a self-administered questionnaire. Ethical approval for the study was granted by the Newcastle and North Tyneside 2 NHS Research Ethics Committee on 15/02/2015 (reference ID: 15/NE/0060).

Participants

Members of the general population, as well as GPs (primary care physicians) and gastroenterology specialists (gastroenterologists or colorectal surgeons) were recruited. Within the general population the inclusion criteria were: men and women aged 18 years or above; living in the UK; with the ability to consent; with or without self-reported constipation; and the exclusion criteria were: individuals with severe gastrointestinal diseases (e.g. inflammatory bowel disease); pregnancy or lactation; and individuals who were also health professionals. Within the doctors group (GPs and specialists) the inclusion criteria were: being in current clinical contact with patients; and living in the UK. For the gastroenterology specialists group, both registrars (fellows) and consultants (attending physicians) in either gastroenterology or colorectal surgery were eligible.

An opportunistic and random sampling technique was adopted using a wide variety of approaches to maximise the sampling frame. Several evidence-informed approaches to increase response rates and limit response bias were adopted, including non-monetary incentives to participate, personalised

invitation emails sent to doctors, and advertisements stating the number of participants recruited to date[21].

The general population were recruited via circular emails and advertising in eight UK universities, on advertising websites, in magazines, in newspapers and via healthy volunteer databases across the UK. As the purpose of this study was to assess perceptions of constipation in both those with and without self-reported constipation (rather than measure prevalence of constipation), attempts were made to specifically target sufficient people with self-reported constipation in the advertisements. This was achieved by including the word "constipation" in advertising text to draw interest from people with constipation and individual emails were also sent to subjects with chronic constipation identified from a previous research project.

GPs were recruited via an advert placed in the monthly newsletter of the Royal College of General Practitioners, and individual personalised emails were sent to all members of the Primary Care Society for Gastroenterology (n=475). Furthermore, 90 GP practices in South and East London were contacted by telephone and/or attended in person and 34 GP meetings in Greater London were attended, where paper questionnaires were distributed for completion.

Specialist doctors were recruited through personalised emails sent to all members of the British Society of Gastroenterology (n=2,202) and all members of the Association of Coloproctology (n=668). Two gastroenterology conferences were attended in person where paper questionnaires were distributed for completion.

Questionnaire

In the absence of a previously validated questionnaire, a new questionnaire was developed to investigate perceptions of constipation diagnosis and agreement with the Rome IV diagnostic criteria. The self-administered questionnaire included closed-ended questions and free-text boxes. The questionnaire was available online for the general population, whereas both online and paper copies

were available for GPs and specialist doctors to facilitate face-to-face recruitment. The questionnaire included four sections: (1) constipation diagnosis and burden, (2) constipation case studies, (3) bowel habits and (4) demographics (example for the general population is provided in Supplementary Material).

Members of the general population were required to provide information regarding age, gender, education, and ethnicity. GPs and specialist doctors provided information regarding gender and ethnicity to enable demographic comparisons.

Constipation diagnosis

In the general population, the presence/absence of self-reported constipation was determined ('do you consider yourself to have constipation'), with those responding positively forming the 'self-reported constipation' subgroup. The presence/absence of chronic functional constipation was also determined (after the self-report question) based upon Rome IV criteria, in which information on usual stool frequency and consistency was reported using the Bristol Stool Form Scale[22], along with the presence of specific symptoms (e.g. 'for at least 25% (one-quarter) of bowel movements I pass, I need to strain a lot'). In this study, meeting the Rome criteria for constipation-predominant irritable bowel syndrome (IBS-C) did not preclude people from meeting criteria for chronic functional constipation; the reason is that the Rome criteria now recognise these two bowel disorders as belonging to the same spectrum, and that they frequently overlap[7]. In fact, it has been confirmed that the sensitivity of the Rome criteria for chronic functional constipation is higher when an overlap with IBS-C is permitted[13].

Perceptions of constipation symptoms

In all groups (general population, GPs, specialist doctors), perceptions of constipation diagnosis were measured by participants being asked to choose up to five symptoms they considered to be the most important for a diagnosis of constipation from a list of 33 symptoms. The 33 symptoms comprised 31

identified during our previous qualitative study[18], to encompassed all symptoms experienced by patients with chronic constipation, as well as symptoms included in the Rome IV criteria and the Cleveland Clinic Constipation Score. Two additional symptoms, not previously associated with constipation ('abdominal rash', 'blurred vision') were included as negative controls. On the online version of the questionnaire these 33 symptoms were presented in random order in order to reduce order bias.

Burden of constipation

In the general population with self-reported constipation, the prevalence of symptoms they experienced, together with their burden, was assessed using the same list of 33 symptoms described above. Those with self-reporting constipation were asked to indicate all symptoms they experienced, and then rate their burden using a 4-point Likert scale (0=not at all bothersome, 1=mildly bothersome, 2= moderately bothersome, 3=severely bothersome).

GPs and specialist doctors were also asked to use the same list of 33 symptoms to indicate up to five symptoms they believe patients with constipation find the most bothersome.

Constipation case studies

In all groups (general population, GPs, specialist doctors), the perception of constipation symptoms to identify the presence/absence of constipation and the agreement with the Rome IV criteria was measured using a case-study approach. Participants were presented in turn with 10 case-studies describing the presence or absence of all Rome IV symptoms: stool frequency, stool consistency (displayed using an image from the Bristol Stool Form Scale), sensation of incomplete evacuation, sensation of anorectal blockage, need for manual maneuvres, and need to strain[7]. The presence or absence of bloating was also added, despite not being part of the Rome IV criteria, as it has been identified as one of the most bothersome symptoms by patients with chronic constipation[20]. Of the 10 case studies, one had no symptoms included in the Rome IV criteria (negative control), five included

one symptom, one included two symptoms, two included three symptoms, and one included all six symptoms of the Rome IV criteria, in addition to abdominal bloating (positive control). Overall, 4 of the 10 case studies fulfilled Rome IV criteria for functional constipation. Participants were presented each case study in turn and were asked whether they would consider each case study as having constipation using a dichotomous response set (yes/no) (Supplementary Material).

The sample size calculation was based on the margin of random sampling error[23, 24]. In order to generate a margin of error of <5% at a 95% confidence level, it was calculated that a sample size of 900 members of the general population, 400 GPs and 325 specialist doctors was required.

Statistical analysis

Associations between counts and other categorical variables were assessed using a Chi-squared test. For continuous data, an ANOVA (for normally distributed data) or Kruskal-Wallis test (for non-normally distributed data) were used to assess differences between the study groups. The symptoms considered important for a diagnosis of constipation were subjected to principal component analysis (PCA) to identify clusters of symptoms that are reported together (correlated). Components were retained where eigenvalues were >1[25], and by using the scree plot[26]. The oblique direct oblimin rotation method was used to help interpretation of the components and clusters of symptoms. Statistical analysis was performed on SPSS (version 22, IBM) and a P value <0.05 was considered statistically significant.

RESULTS

Participant characteristics

Overall, 2,557 members of the general population, 411 GPs (primary care physicians) and 365 specialist doctors were eligible and completed the questionnaire fully, thus satisfying the target sample size (Figure 1). The specialist doctors comprised 224 (61%) gastroenterologists and 141 (39%) colorectal surgeons, of whom 269 (74%) were consultants (attending physicians) and 96 (26%) were

registrars (fellows). The general population group comprised 1,950 (76%) females, while only 211 (51%) of GPs and 102 (28%) of specialist doctors were females ($p<0.001$). In the general population, there were significantly more participants of Caucasian background (2,233, 87%), compared to GPs (197, 48%) and specialist doctors (244, 67%; $p<0.001$). The participants' demographics are presented in Table 1.

Constipation diagnosis

Of the 2,557 members of the general population, 934 self-reported constipation and 1,623 did not. Of the 934 with self-reported constipation, 877 (94%) also met the Rome IV criteria for functional constipation, whereas of the 1,623 who did not self-report constipation, 473 (29%) actually met the Rome IV criteria (Table 2). Based upon self-reports of constipation, this represents a sensitivity of the Rome IV criteria of 94% and a specificity of 71% (Table 2).

Participants who self-reported constipation and met the Rome IV criteria had the lowest stool frequency and hardest stools compared to the other groups (Table 1). Individuals who did not self-report constipation, but met the Rome IV criteria, had a mean stool frequency of 7.6 bowel movements per week.

Perceptions of constipation symptoms

The symptoms considered to be important for a diagnosis of constipation are shown in Table 3. Twenty nine of the 31 symptoms differed in the frequency of being considered important among the general population, GPs and specialist doctors (Table 3). Notably, less than half of the general population considered any of the Rome IV symptoms important for diagnosing constipation (Table 3). For example, 'manual maneuvres' and sense of incomplete evacuation were reported as important by less than 20% of individuals in each group (Table 3). The symptom most frequently considered important for a diagnosis of constipation by the general population was 'straining' (1,080, 42%), by GPs was 'hard stools' (271, 66%) and by specialist doctors was 'infrequent bowel movements' (238, 65%). In contrast,

less than half of GPs (169, 41%) and only a quarter of the constipated general population (697, 27%) ($p<0.001$) considered 'infrequent bowel movements' important for a diagnosis.

There were significant differences in the majority of symptoms considered important for a diagnosis of constipation among the four sub-groups of the general population. In those with self-reported constipation who also met the Rome IV criteria, the symptoms most frequently considered important in diagnosing constipation were 'straining' (362, 41%), 'the need to use laxatives' (298, 34%) and 'hard stools' (285, 33%), whereas those with self-reported constipation not meeting the Rome IV criteria these were 'hard stools' (16, 28%), 'sense of incomplete evacuation' (16, 28%) and 'abdominal discomfort' (16, 28%).

In those without self-reported constipation who either met the Rome IV criteria or those who did not, the symptoms most frequently considered important in diagnosing constipation were the same: 'straining' (197, 42%; 507, 44%; respectively); 'spending a long time on the toilet without a bowel movement' (165, 41%; 492, 43%; respectively) and 'the need to use laxatives' (154, 33%; 446, 39%; respectively). These latter two symptoms are not part of the Rome IV diagnostic criteria.

Symptoms considered important for a diagnosis of constipation were subjected to PCA. Visual inspection of the scree plot indicated that seven principal components (corresponding to seven potential clusters of symptoms) should be retained (see Supplementary Figure 1); all cluster were examined by the authors and were identified to be clinically meaningful (expect for cluster 7 which represented an incorrect diagnosis; Figure 2). The seven clusters are described in Box 1 and explained only 3.5-6.2% of the total variance; some of these were bipolar (i.e. included mutually exclusive symptoms), and comprised of the following symptoms:

- **Cluster 1 (6.2% variance): IBS symptoms** (abdominal discomfort, abdominal pain and bloating); mutually exclusive from symptoms of difficult defecation (manual maneuvers, straining, spending long time on the toilet with a bowel movement, stool getting stuck half way out);
- **Cluster 2 (4.5% variance)**: **rectal discomfort** (rectal bleeding with or after a bowel movement, pain during a bowel movement, and rectal pain or burning after bowel movement); mutually exclusive from infrequent bowel movements;
- **Cluster 3 (3.9% variance)**: **infrequent bowel movements and hard stools**; mutually exclusive from symptoms of unsuccessful defecation (frequent visits to the toilet without a bowel movement, and spending long time on the toiler without a bowel movement);
- **Cluster 4 (3.8% variance)**: **sensory dysfunction** (no sensation of having had a bowel movement, no sense of urge to pass a stool, small stool quantity, sense of incomplete evacuation, and irregular bowel movements);
- **Cluster 5 (3.7% variance): flatulence and bloating** (wind/flatulence, noisy or smelly wind, abdominal bloating, and frequent visits to toilet with a bowel movement); mutually exclusive from the need for laxative use;
- **Cluster 6 (3.5% variance): fecal incontinence** (uncontrolled leakage of stool after a bowel movement, wearing pads to protect against leakage, and rectal bleeding that is not associated with a bowel movement);
- **Cluster 7 (4.3% variance): incorrect diagnosis** (blurred vision, skin rash on abdomen, headache and/or dizziness, backache, and reflux or nausea). This was identified by PCA because only a small proportion of respondents (0%-7%) selected these symptoms as important and, hence, were outliers and significantly contributed to the total variance.

Box 1: The seven clusters of symptoms that tended to be reported together for a diagnosis of constipation as identified through principal component analysis.

Burden of constipation

In those with self-reported constipation, the most prevalent symptom actually experienced was 'hard or lumpy stools' (595, 64%). However, the symptom considered to be most bothersome was 'straining' (491, 53%) (Table 4), and this was the only symptom in the top five most bothersome symptoms for the general population that is also part of the Rome IV criteria. GPs and specialist doctors perceived two of the Rome IV symptoms to be bothersome ('straining', 'manual maneuvers').

Constipation case studies

The findings regarding the effect of various symptoms on perceptions of the presence/absence of constipation based on case studies are presented in Table 5.

In case studies 1 to 6, where constipation was absent based on Rome IV criteria, the rates of correct diagnosis ranged from 66% to 99% (Table 5). As expected, the highest rates for correct diagnosis were where all symptoms were absent (case study 1, negative control) (98%-99%, p=0.207).

In case studies 7-10, where constipation was present based on Rome IV criteria, the rates of correct diagnosis ranged from 39% to 99% (Table 5). As expected, the highest rates for correct diagnosis were where all symptoms were present (case study 10, positive control) (95-99%), although this was still significantly different between groups (p=0.009) (Table 5). Notably, only 39% of specialist doctors correctly identified the presence of constipation in case study 7 ('infrequent bowel movements', 'hard stools'), compared to 49% of the general population and 49% of GPs (p=0.002). Similarly, only 40% of specialist doctors correctly identified constipation in case study 8 ('incomplete evacuation', 'straining', 'manual maneuvres'), compared to 60% of the general population and 63% of GPs (p<0.001). Conversely, only 53% of the general population correctly identified constipation in case study 9 ('hard stools', 'bloating', 'sense of anorectal blockage'), compared to 73% of GPs and 66% of specialist doctors (p<0.001).

Further analysis showed that only 113 (4%) of the general population, 18 (4%) GPs and 20 (5%) specialist doctors correctly identified the presence or absence of constipation in all 10 case studies (p=0.652) (Table 6). Specialist doctors correctly diagnosed fewer constipation case studies compared to the general population and GPs (p<0.001). This is despite constipation being diagnosed more frequently by specialist doctors (mean 3.9 case studies, SD 1.5) (irrespective of whether this was the correct diagnosis or not) compared to the general population (3.3 case studies, SD 1.4) and GPs (3.7 case studies, SD 1.6; p<0.001).

DISCUSSION

This study has illustrated substantial differences in the symptoms perceived to be important for a diagnosis of constipation among the general population, GPs (primary care physicians) and specialist doctors. Importantly, the findings revealed that a variety of different symptoms are deemed important for a diagnosis of constipation by the general population and yet these are not part of current diagnostic criteria or assessment tools. Further, there is no consistent agreement between perceptions of a diagnosis of constipation and the Rome IV criteria. This results in relatively low sensitivity and specificity of the Rome IV criteria when the general population self-diagnose constipation, whilst even GPs and specialist doctors are less accurate in using Rome IV criteria in diagnosing the presence of constipation than its absence.

Constipation diagnosis

Although this study revealed a high sensitivity regarding the Rome IV criteria (94%), specificity was relatively low (71%) when compared to patient self-report. Similar findings were reported in a survey in Asian countries, which reported a sensitivity of 86%, and a lower specificity of 73% of the Rome III criteria when compared with patient self-report[27]. This finding indicates that even though some people do not believe they have constipation, they would still fulfil the formal diagnostic criteria for

chronic constipation. One explanation could be the discordance in symptoms perceived to be important for a diagnosis of constipation and the symptoms included in Rome IV criteria.

'Infrequent bowel movements' was variably reported as important for a diagnosis of constipation, with specialist doctors more frequently considering this symptom important than the general population and GPs. 'Hard stools' was reported as being important for a diagnosis of constipation by the vast majority of GPs and specialist doctors, in contrast to only a quarter of the general population. The symptoms most frequently reported as important for a diagnosis by both general and specialist doctors (i.e. 'infrequent bowel movements' and 'hard stools') agree with previous studies including an Israeli study reporting the majority of primary care physicians defined constipation as "defecation every 4 days or less frequently"[14], and a qualitative study of nine GPs in the UK reporting a focus on stool frequency and consistency[15]. In addition, to what is observed in clinical practice, stool frequency is also a key eligibility criterion in constipation research studies, with many trials in chronic constipation using a modified version of the Rome IV criteria specifically requiring infrequent bowel movements (<3 per week) as an inclusion criterion[28]; this affords greater homogeneity among trial participants [28]. However, patients experience a wide range of different constipation-related symptoms that do not necessarily include infrequent bowel movements[18]; in the current study, only half of those with self-reported constipation experienced this symptom. Hence, use of infrequent bowel movements in clinical trials as an eligibility criterion likely excludes an important cohort of patients who are constipated but have normal stool frequency, particularly those complaining primarily of symptoms of an evacuation disorder[6]. This may limit the ability to extrapolate findings from such trials to patients with constipation who do not have infrequent bowel movements[28].

The symptoms most frequently reported as important for a constipation diagnosis by the general population were 'straining', followed by 'spending a long time on the toilet without passing a stool' and 'the need to use laxatives'. This is, in part, in agreement with a previous Swedish population survey reporting laxative use as the most common perception of constipation[17]. However, significant

differences were found in symptoms perceived to be important for a diagnosis among members of the general population with and without self-reported constipation who fulfilled or did not fulfil Rome IV criteria. In particular, more people with self-reported constipation who also fulfilled the Rome IV criteria reported 'bloating' as an important symptom for diagnosing constipation compared to the other study groups. This finding is interesting as bloating has been considered a supportive symptom of constipation, but is not part of recognised diagnostic criteria, mainly due to its widespread prevalence across different chronic bowel disorders. Bloating was experienced by the majority with self-reported constipation, and was the fourth most common and most bothersome constipation-related symptom[20]. Bloating has been associated with worse QoL, treatment satisfaction and treatment responsiveness in patients with chronic constipation, highlighting the importance and burden of this symptom to patients [29].

Nevertheless, no single symptom was universally considered important for a constipation diagnosis by a majority of the general population. Indeed, the most frequently cited symptom required for a diagnosis of constipation ('straining') was only reported by 42% of the general population, and perceptions of constipation diagnosis in the general population were variable. This heterogeneity in symptoms perceived as important may partly explain the difficulty in devising diagnostic criteria and assessment tools that fully reflect symptom prominence. One option is to use patient-reported outcome measures (PROMs) in clinical practice. PROMs are "any report of the status of a patients' health condition that comes directly from the patient, without interpretation of the patient's response by a clinician…"[30]. Indeed, there has been an increase in the interest of the use of PROM in gastrointestinal disorders in clinical practice and in research[31]. This would facilitate the examination and management of symptoms that are considered important and/or bothersome by the patient, rather than focusing on what the clinician feels is important.

The lack of a sole symptom used to universally diagnose constipation and the lack of consensus among the general population and by doctors highlights that constipation is viewed as a cluster of several

symptoms. This was investigated using a principal component analysis (PCA), revealing six clusters that tended to be reported together for a diagnosis of constipation (and an additional cluster reported by very few participants consisting of negative control symptoms). Importantly, although some clusters included symptoms present in the Rome IV criteria (and other diagnostic criteria), the majority of the clusters included symptoms that are not part of any formal diagnostic criteria. Of particular interest were clusters including several symptoms of rectal discomfort (cluster 2), sensory dysfunction (cluster 4) and fecal incontinence (cluster 6). Each of these are common symptoms reflecting different pathophysiologies and aetiologies of chronic constipation, such us rectal hyposensitivity and pelvic floor dysfunction[32], which are not currently represented in the formal diagnostic criteria for chronic constipation *per se*. Instead, the Rome IV criteria have a separate chronic bowel disorder classification for such symptoms called "Defecation disorders"[33], which require complementary diagnostic tests to make the diagnosis, which are not always available, particularly in primary care.

Indeed, the use of specialised diagnostic tests, such as gut transit studies and defecografy[34], may improve the diagnostic accuracy of constipation by identifying underlying pathophysiological mechanisms, including dysmotility, sensory dysfunction and evacuation disorders[33]. Nevertheless, constipation is, by definition, a disorder based on symptoms[7], and therefore comprehensive and appropriate assessment of symptoms is still crucial for screening and identifying constipation in both the clinical and research setting, especially where such specialised diagnostic tests may not be available.

It is important to note however that the seven clusters that were generated in the PCA explained only 30% of total variance of the participants' responses. The small amount of total variance explained by the clusters may relate to the wide range of symptoms and possible permutations of symptoms. The high individuality of the general population's responses was probably also reflected on participants' individual component scores for each cluster. Again, this reinforces the use of PROMs for the identification and diagnosis of constipation in clinical practice and research.

There are several potential factors contributing to the difference in the symptoms perceived to be important for a diagnosis of constipation among the general population, GPs and specialist doctors. These could include the influence of medical education and clinical experience of doctors versus the general population, but also the influence of cultural and ethnicity differences among these groups. In fact, this study showed that there were significantly more GPs of an Asian/Asian British ethnicity compared to the general population and specialist doctors, who were primarily Caucasian.

When the Rome IV criteria were assessed based on case studies, the majority of participants across all groups correctly identified the *absence* of constipation, but when constipation was present (based upon Rome IV), a great proportion of the general population, GPs and specialist doctors failed to make a correct, positive diagnosis. The study also revealed that unless all six symptoms of the Rome IV criteria were present, only 39%-73% of individuals correctly diagnosed the presence of constipation.

Although 'infrequent bowel movements' and 'hard stools' were among the symptoms that were most frequently reported as being important for a diagnosis of constipation by GPs and specialist doctors, when asked to diagnose a case study which had both of these (and hence fulfilled the Rome IV criteria for constipation) (case study 7), the majority of respondents failed to correctly identify constipation (51% to 61%). This is of major importance as it shows a discrepancy between the perceived symptoms that are considered to be important for a diagnosis by the doctors, and what actually happens in clinical practice.

Strengths and limitations

A strength of this large study is the use of a robust statistical technique, PCA, to identify clusters of symptoms considered to be important for a diagnosis of constipation. In addition, the use of a comprehensive list of 33 symptoms (including two negative control symptoms) allowed the identification of those that are considered to be important for a diagnosis of constipation that have not been reported in previous surveys as important for a diagnosis or diagnostic criteria before (e.g. 'spending a long time in the toilet without being able to pass a stool', 'rectal pain'). Furthermore, this

is the first study to assess the diagnosis of constipation of case studies based on current formal diagnostic criteria, indirectly assessing the current clinical practice.

A limitation of this study is the use of an internet-based survey which is known to introduce selection biases[35]. Response bias is likely a potential issue, despite efforts to encourage comprehensive responses. In addition, the sampling techniques targeted both constipated and non-constipated populations and, therefore, this survey is not suitable for the measurement of prevalence data for a constipation diagnosis. The use of a quantitative cross-sectional design does not allow capture of the complete perceptions of the study participants, and could not provide data to justify the perceptions recorded here.

Conclusion

This study has revealed that a variety of symptoms are considered important for a diagnosis of constipation by the general population that are not part of any current diagnostic criteria or assessment tools, with significant differences between the general population and doctors. This is of major importance as it may mean that patients who seek medical care for their constipation-related symptoms may not have their symptoms recognised as constipation by the doctor and, therefore, may not be examined, diagnosed or managed as such. This could significantly impact patients' access to care and management, as well as availability and access to treatment. This reinforces the potential for using PROMs in clinical practice to accurately reflect patients' individual needs and concerns. Finally, there is no consistent agreement between perceptions of diagnosis of constipation and the Rome IV criteria and these criteria are not always applied correctly. These findings emphasize the need to re-define the current universally accepted diagnostic criteria so they reflect patients' and doctors' perceptions. Education of the general population on the formal diagnostic criteria for constipation is needed, while education of health care professionals is also warranted regarding what patients perceive important for a diagnosis of constipation so that the most burdensome of symptoms can be adequately managed.

REFERENCES

1. Emmanuel A, Quigley EM, Simren M, et al., Factors affecting satisfaction with treatment in European women with chronic constipation: An internet survey. *United European Gastroenterol J.* 2013;1(5): 375-84.
2. Everhart JE and Ruhl CE, Burden of digestive diseases in the United States part I: overall and upper gastrointestinal diseases. *Gastroenterology.* 2009;136(2): 376-86.
3. Nellesen D, Yee K, Chawla A, et al., A systematic review of the economic and humanistic burden of illness in irritable bowel syndrome and chronic constipation. *J Manag Care Pharm.* 2013;19(9): 755-64.
4. Shafe AC, Lee S, Dalrymple JS, et al., The LUCK study: Laxative Usage in patients with GP-diagnosed Constipation in the UK, within the general population and in pregnancy. An epidemiological study using the General Practice Research Database (GPRD). *Therap Adv Gastroenterol.* 2011;4(6): 343-63.
5. Health and Social Care Information Centre. *National Statistics Hospital Episode Statistics, Admitted Patient Care, England - 2013-14.* 2015 28 January 2015]; Available from: http://www.hscic.gov.uk/searchcatalogue?productid=17192&q=title%3a%22Hospital+Episode+Statistics%2c+Admitted+patient+care+-+England%22&sort=Relevance&size=10&page=1#top.
6. Cook IJ, Talley NJ, Benninga MA, et al., Chronic constipation: overview and challenges. *Neurogastroenterol Motil.* 2009;21 Suppl 2: 1-8.
7. Mearin F, Lacy BE, Chang L, et al., Bowel Disorders. *Gastroenterology.* 2016;150(6): 1393-1407.
8. Soh AYS, Kang JY, Siah KTH, et al., Searching for a definition for pharmacologically refractory constipation: A systematic review. *J Gastroenterol Hepatol.* 2018;33(3): 564-575.
9. Quigley EM, Editorial: differentiating chronic idiopathic constipation from constipation-predominant irritable bowel syndrome--possible and important? *Aliment Pharmacol Ther.* 2015;41(12): 1299.
10. Agachan F, Chen T, Pfeifer J, et al., A constipation scoring system to simplify evaluation and management of constipated patients. *Dis Colon Rectum.* 1996;39(6): 681-5.
11. Frank L, Kleinman L, Farup C, et al., Psychometric validation of a constipation symptom assessment questionnaire. *Scand J Gastroenterol.* 1999;34(9): 870-7.
12. Suares NC and Ford AC, Prevalence of, and risk factors for, chronic idiopathic constipation in the community: systematic review and meta-analysis. *Am J Gastroenterol.* 2011;106(9): 1582-91.
13. Palsson OS, Whitehead WE, van Tilburg MAL, et al., Development and Validation of the Rome IV Diagnostic Questionnaire for Adults. *Gastroenterology.* 2016;150(6): 1481-1491.
14. Herz MJ, Kahan E, Zalevski S, et al., Constipation: a different entity for patients and doctors. *Fam Pract.* 1996;13(2): 156-9.
15. Mihaylov S, Stark C, McColl E, et al., Stepped treatment of older adults on laxatives. The STOOL trial. *Health Technol Assess.* 2008;12(13): iii-iv, ix-139.
16. Moore-Gillon V, Constipation: what does the patient mean? *J R Soc Med.* 1984;77(2): 108-10.
17. Walter S, Hallbook O, Gotthard R, et al., A population-based study on bowel habits in a Swedish community: prevalence of faecal incontinence and constipation. *Scand J Gastroenterol.* 2002;37(8): 911-6.
18. Dimidi E, Dibley L, Cotterill N, et al., Validated constipation symptom and quality-of-life measures neither reflect patient and clinician concerns nor use words familiar to patients. *Gastrointestinal Nursing.* 2016;14(7): 29-38.
19. Guerin A, Carson RT, Lewis B, et al., The economic burden of treatment failure amongst patients with irritable bowel syndrome with constipation or chronic constipation: a retrospective analysis of a Medicaid population. *J Med Econ.* 2014;17(8): 577-86.

20. Johanson JF and Kralstein J, Chronic constipation: a survey of the patient perspective. *Aliment Pharmacol Ther.* 2007;25(5): 599-608.
21. Edwards PJ, Roberts I, Clarke MJ, et al., Methods to increase response to postal and electronic questionnaires. *Cochrane Database Syst Rev.* 2009;3(3): MR000008.
22. Blake MR, Raker JM, and Whelan K, Validity and reliability of the Bristol Stool Form Scale in healthy adults and patients with diarrhoea-predominant irritable bowel syndrome. *Aliment Pharmacol Ther.* 2016;44: 693-703.
23. Kalsi T, Payne S, Brodie H, et al., Are the UK oncology trainees adequately informed about the needs of older people with cancer? *Br J Cancer.* 2013;108(10): 1936-41.
24. Barlett JE, Kotrlik JW, and Higgins CC, Organizational research: Determining appropriate sample size in survey research. *Information Technology, Learning, and Performance Journal.* 2001;19(1): 43-50.
25. Kaiser HF, The Application of Electronic-Computers to Factor-Analysis. *Educ Psychol Meas.* 1960;20(1): 141-151.
26. Cattell RB, The Scree Test For The Number Of Factors. *Multivariate Behav Res.* 1966;1(2): 245-76.
27. Gwee KA, Bergmans P, Kim J, et al., Assessment of the Asian Neurogastroenterology and Motility Association Chronic Constipation Criteria: An Asian Multicenter Cross-sectional Study. *J Neurogastroenterol Motil.* 2016;23(2): 262-272.
28. Basilisco G and Coletta M, Chronic constipation: a critical review. *Dig Liver Dis.* 2013;45(11): 886-93.
29. Neri L, Iovino P, and Laxative Inadequate Relief Survey Group, Bloating is associated with worse quality of life, treatment satisfaction, and treatment responsiveness among patients with constipation-predominant irritable bowel syndrome and functional constipation. *Neurogastroenterol Motil.* 2016;28: 581-891.
30. Burke LB, Kennedy DL, Miskala PH, et al., The use of patient-reported outcome measures in the evaluation of medical products for regulatory approval. *Clin Pharmacol Ther.* 2008;84(2): 281-3.
31. Spiegel BMR, Patient-Reported Outcomes in Gastroenterology: Clinical and Research Applications. *J Neurogastroenterol Motil.* 2013;19(2): 137-148.
32. Burgell RE and Scott SM, Rectal hyposensitivity. *J Neurogastroenterol Motil.* 2012;18(4): 373-84.
33. Rao SS, Bharucha AE, Chiarioni G, et al., Functional Anorectal Disorders. *Gastroenterology.* 2016: S0016-5085(16)00175-X.
34. Grossi U, Di Tanna GL, Heinrich H, et al., Systematic review with meta-analysis: defecography should be a first-line diagnostic modality in patients with refractory constipation. *Aliment Pharmacol Ther.* 2018;48(11-12): 1186-1201.
35. Wright KB, Researching Internet-based populations: Advantages and disadvantages of online survey research, online questionnaire authoring software packages, and Web survey services. *J Comput Mediat Commun.* 2005;10(3).

FIGURE LEGENDS

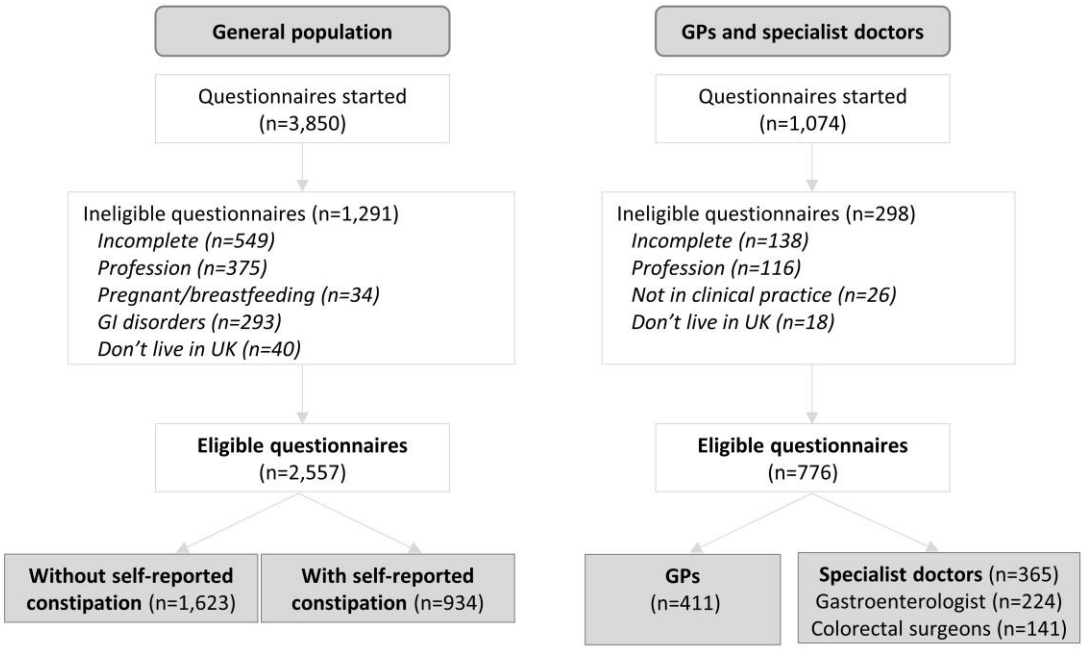
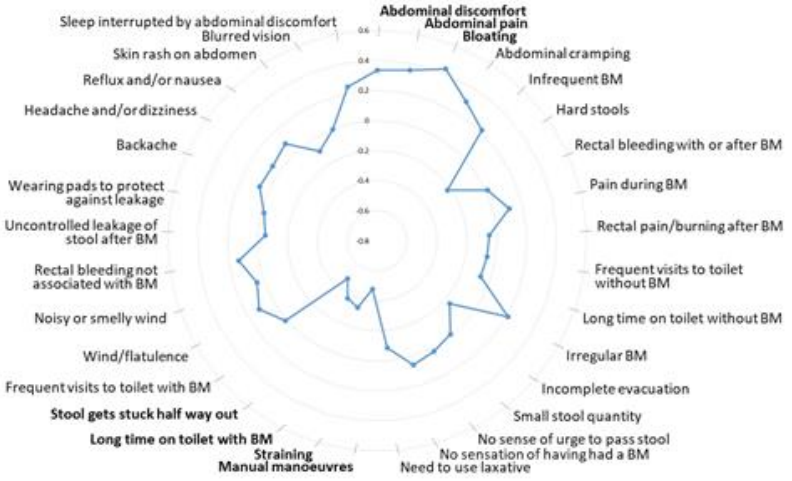
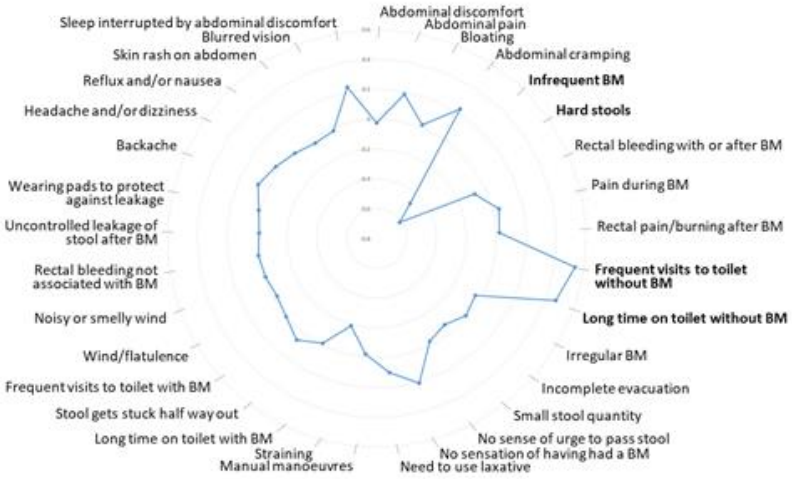


Figure 1: Flow diagram representing the number of questionnaires started and completed.

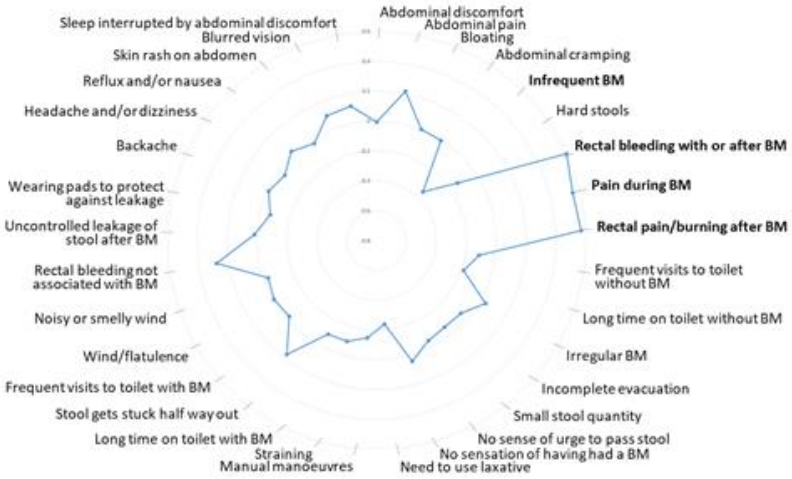
Cluster 1:
IBS symptoms; mutually exclusive from symptoms of difficult defecation



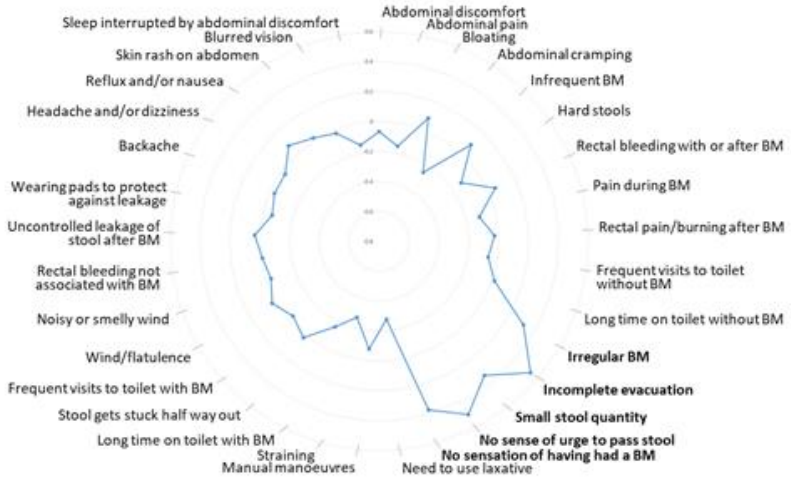
Cluster 2:
Rectal discomfort; mutually exclusive from infrequent bowel movements



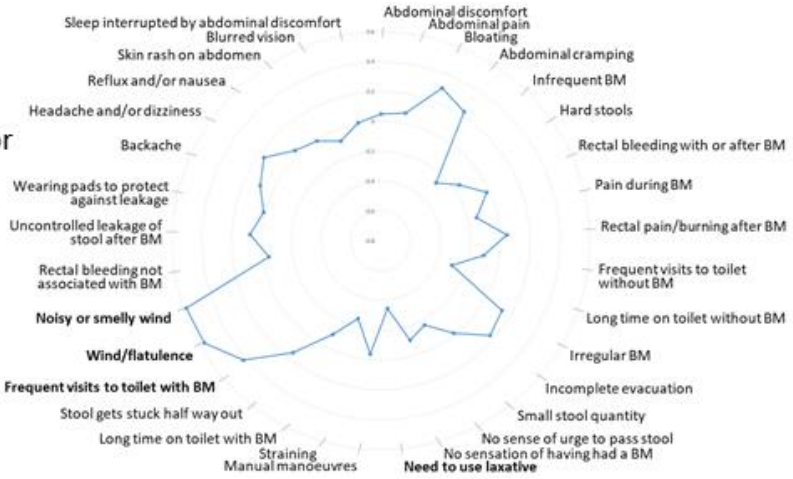
Cluster 3:
Infrequent bowel movements and hard stools; mutually exclusive from symptoms of unsuccessful defecation



Cluster 4:
Sensory dysfunction



Cluster 5:
Flatulence and bloating; mutually exclusive from need for laxative use



Cluster 6:
Fecal incontinence

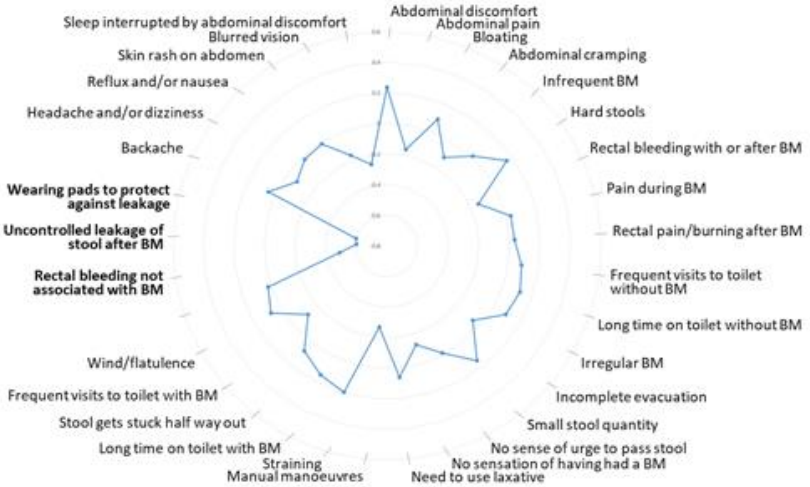


Figure 2: Radar plots representing the loadings of each symptom for each cluster identified in the principal component analysis. Symptoms with a loading greater than ±0.300 (in bold) contribute significantly to the cluster. The positive and negative symbols refer to symptoms that are mutually exclusive within each cluster. Cluster 7 is not depicted as it represents an incorrect diagnosis and is not clinically meaningful.

Table 1: Participant characteristics of the general population, GPs and specialist doctors, and within the general population, participants grouped based on the presence/absence of self-reported constipation and Rome IV constipation

	Total participants (n=3,333)				**General population** (n=2,577)				
					Self-reported constipation (n=934)		**No self-reported constipation** (n=1,623)		
	General population (n=2,557)	**General practitioners** (n=411)	**Specialist doctors** (n=365)	**P value**	**Rome IV criteria +** (n=877)	**Rome IV criteria -** (n=57)	**Rome IV criteria +** (n=473)	**Rome IV criteria -** (n=1,150)	**P value**
Age, years	38.9 (14.2)	-	-	-	40.8 (13.4)[c]	39.4 (14.6)[a,b,c]	35.6 (13.6)[b]	38.7 (14.7)[a]	<0.001†
Females, n (%)	1,950 (76)[a]	211 (51)[b]	102 (28)[c]	<0.001*	778 (89)[c]	44 (77) [a,b,c]	363 (77)[b]	765 (67)[a]	<0.001*
Ethnicity, n (%)									
White (Caucasian)	2233 (87) [a]	197 (48)[b]	244 (67)[c]		769 (88)[a]	45 (79)[a]	403 (85)[a]	1016 (88)[a]	
Asian	164 (6)[a]	159 (39)[b]	87 (24)[c]		49 (6)[a]	5 (9)[a]	28 (6)[a]	82 (7)[a]	
Black	61 (2)[a]	31 (8)[b]	2 (1)[a]	<0.001*	26 (3)[a]	3 (5)[a]	16 (3)[a]	16 (1)[a]	0.048*
Mixed	74 (3)[a]	12 (3)[b]	12 (3)[a]		25 (3)[a]	25 (3)[a]	17 (4)[a]	29 (3)[a]	
Other	25 (1)[a]	12 (3)[a,b]	20 (6)[b]		8 (1)[a]	1 (2)[a]	9 (2)[a]	7 (1)[a]	
Education, n (%)									
No formal qualifications	83 (3)	-	-	-	37 (4)[a]	0 (0)[a]	13 (3)[a]	33 (3)[a]	
Vocational qualifications	261 (10)	-	-	-	135 (15)[b]	6 (11)[a,b]	42 (9)[a]	78 (7)[a]	
School level qualifications	955 (37)	-	-	-	362 (41)[b]	21 (37)[a,b]	180 (38)[a,b]	392 (34)[a]	<0.001*
University degree	820 (32)	-	-	-	246 (28)[b]	21 (37)[a,b]	149 (32)[a,b]	404 (35)[a]	
Postgraduate degree	438 (17)	-	-	-	97 (11)[b]	9 (16)[a,b]	89 (19)[a]	243 (21)[a]	
Stool frequency / week	6.7 (4.6)	-	-	-	4.3 (4.2)[d]	6.5 (5.5)[c]	7.6 (4.6)[b]	8.1 (4.1)[a]	<0.001†
Stool consistency, Bristol stool form scale	3.2 (1.3)	-	-	-	2.5 (1.4)[c]	3.7 (1.5)[b]	3.3 (1.1)[a]	3.7 (0.9)[a,b]	<0.001†

Values are mean (SD), unless specified.

*Chi squared p values.

†Kruskal-Wallis p value across groups.

[a-d]Means in a row within without a common superscript letter significantly differ ($P < 0.05$).

Table 2: Diagnostic sensitivity, specificity and accuracy of definitions of functional constipation in 2,557 members of the general population

	Sensitivity	Specificity	Accuracy	Positive predictive value	Negative predictive value
Rome IV (using self-reports as the gold standard')	94%	71%	79%	65%	95%
Self-report (using Rome IV criteria as the 'gold standard')	65%	95%	79%	94%	71%

Table 3: Symptoms that are considered to be important for a diagnosis of constipation for the three study groups and four general population subgroups.

	Total participants (n=3,333)				**General population** (n=2,577)				
					Self-reported constipation (n=934)		**No self-reported constipation** (n=1,623)		
	General population (n=2,557)	**General practitioners** (n=411)	**Specialist doctors** (n=365)	**P value**	**Rome IV criteria +** (n=877)	**Rome IV criteria -** (n=57)	**Rome IV criteria +** (n=473)	**Rome IV criteria -** (n=1,150)	**P value**
Symptoms in Rome IV criteria									
Straining	1080 (42)[a]	249 (61)[b]	192 (53)[b]	***<0.001***	362 (41)[a,b]	14 (25)[b]	197 (42)[a,b]	507 (44)[a]	***0.025***
Hard stools	726 (28)[a]	271 (66)[b]	209 (57)[c]	***<0.001***	285 (33)	16 (28)	115 (24)	310 (27)	*0.775*
Incomplete evacuation	465 (18)[a]	54 (13)[b]	77 (21)[a]	***0.011***	205 (23)[b]	16 (28)[b]	93 (20)[b]	151 (13)[a]	***<0.001***
Manual maneuvers	370 (15)[a]	140 (34)[b]	118 (32)[b]	***<0.001***	137 (16)	4 (7)	78 (17)	151 (13)	*0.081*
Infrequent BM	697 (27)[a]	169 (41)[a,b]	238 (65)[b]	***<0.001***	230 (26)	12 (21)	123 (26)	332 (29)	*0.326*
Other symptoms									
Abdominal discomfort	608 (24)[a]	124 (30)[b]	52 (14)[c]	***<0.001***	183 (21)[b]	16 (28)[a,b]	109 (23)[a,b]	300 (26)[a]	***0.042***
Abdominal pain	564 (22)[a]	60 (15)[b]	34 (9)[b]	***<0.001***	182 (21)	9 (16)	110 (23)	263 (23)	*0.390*
Abdominal cramping	420 (16)[a]	35 (9)[b]	13 (4)[c]	***<0.001***	124 (14)	6 (11)	82 (17)	208 (18)	*0.061*
Bloating	593 (23)[a]	61 (15)[b]	43 (12)[b]	***<0.001***	259 (30)[b]	14 (25)[a,b]	97 (21)[a]	223 (19)[a]	***<0.001***
Rectal bleeding with or after BM	328 (13)[a]	41 (10)[a]	13 (4)[b]	***<0.001***	153 (17)[c]	12 (21)[b,c]	50 (11)[a,b]	113 (10)[a]	***<0.001***
Rectal bleeding not associated with BM	66 (3)[a]	10 (2)[a]	4 (1)[a]	***<0.001***	23 (3)	2 (4)	12 (3)	29 (3)	*0.974*
Pain during a BM	484 (19)[a]	52 (13)[b]	10 (3)[c]	***<0.001***	157 (18)	16 (28)	93 (20)	218 (19)	*0.276*
Rectal pain or burning after a BM	162 (6)[a]	13 (3)[b]	4 (1)[b]	***<0.001***	63 (7)	4 (7)	19 (4)	76 (7)	*0.136*
Need to use laxative	911 (36)[a]	164 (40)[a]	205 (56)[b]	***<0.001***	298 (34)[a]	13 (23)[a]	154 (33)[a]	446 (39)[a]	***0.007***
Irregular BM	326 (13)[a]	16 (4)[b]	24 (6)[b]	***<0.001***	141 (16)[b]	11 (19)[a,b]	54 (11)[a,b]	120 (10)[a]	***0.001***
Frequent visits to toilet without BM	487 (19)[a]	62 (15)[a,b]	50 (14)[b]	***0.012***	118 (14)[b]	6 (11)[a,b]	102 (22)[a]	261 (23)[a]	***<0.001***
Frequent visits to toilet with BM	56 (2)[a]	2 (1)[a]	4 (1)[a]	***0.031***	17 (2)	2 (4)	17 (4)	20 (2)	*0.104*
Small stool quantity	293 (12)	51 (12)	28 (8)[b]	*0.069*	116 (13)	9 (16)	53 (11)	115 (10)	*0.102*
No sense of urge to pass stool	203 (8)[a]	13 (3)[b]	40 (11)[a]	***<0.001***	74 (8)	6 (11)	36 (8)	87 (8)	*0.775*
Long time on toilet with BM	598 (23)[a]	118 (29)[a,b]	114 (31)[b]	***0.001***	171 (20)[b]	10 (18)[a,b]	127 (27)[a]	290 (25)[a]	***0.003***
Long time on toilet without BM	961 (38)[a]	95 (23)[b]	121 (33)[a]	***<0.001***	261 (30)[b]	13 (22)[b]	195 (41)[a]	492 (43)[a]	***<0.001***
Wind/flatulence	239 (9)[a]	11 (3)[b]	4 (1)[b]	***<0.001***	118 (14)[c]	9 (16)[b,c]	39 (8)[a,b]	73 (6)[a]	***<0.001***
Noisy or smelly wind	208 (8)[a]	10 (2)[b]	2 (1)[b]	***<0.001***	89 (10)[b]	9 (16)[b]	38 (8)[a,b]	72 (6)[a]	***0.002***
Backache	166 (7)[a]	8 (2)[b]	1 (0)[b]	***<0.001***	73 (8)[b]	4 (7)[a,b]	37 (8)[b]	52 (5)[a]	***0.003***
Headache and/or dizziness	93 (4)[a]	3 (1)[b]	1 (0)[b]	***<0.001***	35 (4)[a,b]	6 (11)[b]	24 (5)[b]	28 (2)[a]	***0.001***
Reflux and/or nausea	82 (3)[a]	2 (1)[b]	1 (0)[b]	***<0.001***	38 (4)[a]	4 (7)[a]	12 (3)[a]	28 (2)[a]	***0.027***

	Total participants (n=3,333)				**General population** (n=2,577)				
					Self-reported constipation (n=934)		**No self-reported constipation** (n=1,623)		
	General population (n=2,557)	**General practitioners** (n=411)	**Specialist doctors** (n=365)	**P value**	**Rome IV criteria +** (n=877)	**Rome IV criteria -** (n=57)	**Rome IV criteria +** (n=473)	**Rome IV criteria -** (n=1,150)	**P value**
Uncontrolled leakage of stool after BM	49 (2)[a]	22 (5)[b]	12 (3)[a,b]	***<0.001***	17 (2)	0 (0)	6 (1)	26 (2)	*0.408*
Wearing of pads to protect against leakage	33 (1)[a]	14 (3)[b]	9 (3)[a,b]	***0.004***	8 (1)	0 (0)	12 (3)	13 (1)	*0.052*
Stool gets stuck half way out	403 (16)[a]	48 (12)[a]	14 (4)[b]	***<0.001***	158 (18)	7 (12)	78 (17)	160 (14)	*0.071*
No sensation of having had a BM	66 (3)	4 (1)	9 (3)	*0.137*	18 (2)	1 (2)	16 (3)	31 (3)	*0.494*
Sleep interrupted by abdominal discomfort	175 (7)[a]	3 (1)[b]	3 (1)[b]	***<0.001***	59 (7)	2 (4)	42 (9)	72 (6)	*0.195*
Negative control symptoms									
Skin rash on abdomen	8 (0)	2 (1)	1 (0)	*0.834*	5 (1)	0 (0)	2 (0)	1 (0)	*0.250*
Blurred vision	16 (1)	2 (1)	1 (0)	*0.686*	3 (1)	0 (0)	3 (1)	10 (1)	*0.459*

Values are n (%).

Chi squared tests were performed across groups.

P values in bold were statistically significant.

[a-c]Means in a row without a common superscript letter significantly differ ($P < 0.05$).

BM: bowel movements.

Table 4: Numbers experiencing different symptoms in the general population with self-reported constipation and whether they were considered moderately to severely bothersome, compared to perceived burden by GPs and Specialist doctors.

	General population with self-reported constipation (n=934)				
	Experienced symptoms	Symptoms moderately to severely bothersome	GPs (n=411)	Specialist doctors (n=365)	P value
Symptoms in Rome IV criteria					
Straining	595 (64)	491 (53)	182 (44)	148 (41)	*0.294*
Hard stools	553 (59)	371 (40)	80 (20)	50 (14)	***0.032***
Incomplete evacuation	505 (54)	353 (38)	59 (14)	96 (26)	***<0.001***
Manual maneuvers	229 (25)	202 (22)	130 (32)	126 (35)	*0.393*
Infrequent BM	462 (50)	304 (33)	68 (17)	77 (21)	*0.105*
Other symptoms					
Abdominal discomfort	521 (56)	436 (47)	140 (34)	107 (29)	*0.156*
Abdominal pain	449 (48)	386 (41)	131 (32)	119 (33)	*0.828*
Abdominal cramping	398 (43)	327 (35)	65 (16)	75 (21)	*0.087*
Bloating	531 (57)	452 (48)	130 (32)	154 (42)	***0.002***
Rectal bleeding with or after BM	284 (30)	211 (11)	82 (20)	20 (6)	***<0.001***
Rectal bleeding not associated with BM	29 (3)	20 (2)	13 (3)	5 (1)	*0.098*
Pain during a BM	403 (43)	341 (37)	136 (33)	62 (17)	***<0.001***
Rectal pain or burning after a BM	256 (27)	205 (22)	45 (11)	16 (4)	***0.001***
Need to use laxative	438 (47)	290 (31)	74 (18)	76 (21)	*0.321*
Irregular BM	484 (52)	309 (33)	28 (7)	11 (3)	***0.016***
Frequent visits to toilet without BM	279 (30)	216 (23)	106 (26)	75 (21)	*0.085*
Frequent visits to toilet with BM	74 (8)	56 (6)	5 (1)	7 (2)	*0.429*
Small stool quantity	436 (47)	257 (28)	30 (7)	17 (5)	*0.124*
No sense of urge to pass stool	154 (17)	85 (9)	10 (2)	14 (4)	*0.260*
Long time on toilet with BM	468 (50)	365 (39)	117 (29)	140 (38)	***0.003***
Long time on toilet without BM	479 (51)	380 (41)	105 (26)	121 (33)	***0.020***
Wind/flatulence	436 (47)	317 (34)	47 (11)	29 (8)	*0.103*
Noisy or smelly wind	351 (38)	273 (29)	50 (12)	32 (9)	*0.124*
Backache	270 (29)	203 (22)	8 (2)	6 (2)	*0.752*
Headache and/or dizziness	181 (19)	133 (14)	0 (0)	4 (1)	***0.033***
Reflux and/or nausea	200 (21)	163 (18)	7 (2)	3 (1)	*0.277*
Uncontrolled leakage of stool after BM	48 (5)	39 (4)	39 (10)	45 (12)	*0.204*
Wearing of pads to protect against leakage	36 (4)	27 (3)	29 (7)	38 (10)	*0.097*
Stool gets stuck half way out	392 (42)	322 (34)	40 (10)	25 (7)	*0.148*
No sensation of having had a BM	74 (8)	51 (6)	2 (1)	10 (3)	***0.011***
Sleep interrupted by abdominal discomfort	195 (21)	162 (17)	21 (5)	18 (5)	*0.910*
Negative control symptoms					
Skin rash on abdomen	12 (1)	7 (1)	1 (0)	1 (0)	*0.933*
Blurred vision	45 (5)	29 (3)	1 (0)	2 (1)	*0.495*

All values are n (%).

Chi squared tests were performed across groups for the bothersome rating.

BM: bowel movements.

Shading indicates the top 5 symptom in each group.

Table 5: Constipation diagnosis based on case studies. A comparison of percentages of correct diagnosis of constipation based on the Rome IV criteria.

	Stool frequency (stools per week)	Stool consistency (Bristol stool form scale)	Bloating	Incomplete evacuation	Straining	Sense of anorectal blockage	Manual maneuvers	Total participants (n=3,333)				General population (n=2,577)				
												Self-reported constipation (n=934)		No self-reported constipation (n=1,623)		
								General population (n=2,557)	General practitioners (n=411)	Specialist doctors (n=365)	P value	Rome IV criteria + (n=877)	Rome IV criteria - (n=57)	Rome IV criteria + (n=473)	Rome IV criteria - (n=1,150)	P value
Non-constipated case studies (Rome IV)																
1	7	Type 4	No	No	No	No	No	2495 (98)	404 (98)	361 (99)	*0.207*	857 (98)	56 (98)	459 (97)	1123 (98)	*0.853*
2	2	Type 4	No	No	No	No	No	2141 (84)[a]	378 (92)[b]	341 (93)[b]	***<0.001***	756 (86)	45 (79)	386 (82)	954 (83)	*0.073*
3	7	Type 1	No	No	No	No	No	2035 (80)[a]	297 (72)b	314 (86)[c]	***<0.001***	659 (75)[b]	42 (74)[a,b]	386 (82)[a]	948 (82)[a]	***<0.001***
4	7	Type 4	Yes	No	No	No	No	2415 (94)	388 (94)	354 (97)	*0.122*	821 (94)	52 (91)	443 (94)	1099 (96)	*0.133*
5	7	Type 4	No	Yes	No	No	No	2327 (91)	366 (89)	342 (94)	*0.075*	787 (90)	49 (86)	437 (92)	1054 (92)	*0.159*
6	7	Type 4	No	No	Yes	No	No	2005 (78)[a]	272 (66)[b]	302 (83)[a]	***<0.001***	687 (78)[a]	40 (70)[a]	390 (83)[a]	888 (77)[a]	***0.050***
Constipated case studies (Rome IV)																
7	2	Type 1	No	No	No	No	No	1245 (49)[a]	201 (49)[a]	142 (39)[b]	***0.002***	461 (53)[b]	31 (54)[a,b]	228 (48)[a,b]	525 (46)[a]	***0.016***
8	7	Type 5	No	Yes	Yes	No	Yes	1523 (60)[a]	260 (63)[a]	144 (40)[b]	***<0.001***	543 (62)	38 (67)	277 (59)	665 (58)	*0.183*
9	7	Type 1	Yes	No	No	Yes	No	1362 (53)[a]	103 (73)[b]	240 (66)[b]	***<0.001***	517 (59)[b]	35 (61)[a,b]	241 (51)[a]	569 (50)[a]	***<0.001***
10	2	Type 1	Yes	Yes	Yes	Yes	Yes	2467 (97)[a]	405 (99)[b]	345 (95)[a]	***0.009***	857 (98)	55 (97)	456 (96)	1099 (96)	*0.078*

All values are n (%).

*Chi squared p values.

Shading shows constipation-related symptom present per case study.

Case studies 1-10 were not presented in the same order in the questionnaire as they are presented in this table, so that there was no observable pattern in the severity or number of symptoms included in each case study.

[a-c]Means in a row within Section A and B without a common superscript letter significantly differ ($P < 0.05$)

Table 6: Proportion of the case studies that were correctly diagnosed

	General population (n=2557)	GPs (n=411)	Specialist doctors (n=365)	P value
All case studies	78% (11)[a]	79% (10)[a]	79% (10)[a]	***0.041***
Non-constipated (case studies 1-6)	87% (17)[a]	85% (17)[b]	92% (13)[c]	***<0.001***
Constipated (case studies 7-10)	65% (25)[a]	70% (23)[b]	60% (25)[c]	***<0.001***

Data are mean (SD) percentage of correctly diagnosed case studies.

[a-c] Means in a row without a common superscript letter significantly differ (P < 0.05).